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1: J Immunol. 1987 Feb 1;138(3):720-5.

Activation of human B cell proliferation through surface Bp35 (CD20) polypeptides or immunoglobulin receptors.

Clark EA, Shu G.

Human B cells can be activated with monoclonal antibodies (mAb) to surface IgM receptors or mAb to a 35-kilodalton B cell differentiation antigen, Bp35 (CD20). We compared anti-Ig-induced B cell activation with B cell triggering by anti-Bp35. Both anti-Ig- and anti-Bp35-dependent proliferation were augmented by the same co-stimulants, including a partially purified BCGF, recombinant IL 1, TPA, or each other. When anti-Bp35 and anti-Ig were used together to induce proliferation of tonsillar B cells, the strongest response was observed when anti-Bp35 was added 12 to 24 hr before anti-Ig. Anti-Bp35 also was found to act most effectively when added before the BCGF. Blood and tonsillar B cells differed in their proliferative response to anti-Ig or anti-Bp35: unlike dense tonsillar B cells, which consistently proliferated in response to either stimulus, blood B cells from many donors proliferated in response to anti-Ig but not to anti-Bp35 even in the presence of other co-stimuli. Dense tonsillar B cells that proliferate in response to anti-Bp35 appeared to be at a more activated stage than unresponsive blood B cells because they expressed higher levels of HLA class II molecules than blood B cells. Pretreatment of blood B cells with anti-Bp35 converted them to an HLA-DR(bri) phenotype and made them more responsive to anti-Ig-induced proliferation. These results suggest that B cells at different stages of differentiation differ in their response to anti-Bp35 and anti-Ig. The Bp35 surface polypeptide may play an early role in the activation of B cells prior to antigen or other signals.

PMID: 3492530 [PubMed - indexed for MEDLINE]

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1: J Immunol. 1989 Apr 1;142(7):2560-8.

Structure of the gene encoding the human B lymphocyte differentiation antigen CD20 (B1).

Tedder TF, Klejman G, Schlossman SF, Saito H.

Division of Tumor Immunology, Dana-Farber Cancer Institute, Boston, MA 02115.

The CD20 (B1) molecule is a differentiation Ag found only on the surface of B lymphocytes. This structurally unique phosphoprotein plays a role in the regulation of human B cell proliferation and differentiation. In this report genomic DNA clones containing the human CD20 gene were isolated and the structure of the CD20 gene determined. Southern blot analysis revealed that CD20 mRNA was transcribed from a single-copy gene. The CD20 gene was 16 kb long and was composed of eight exons. The first exon marked the major transcription initiation site as determined by primer extension and S1 nuclease analysis. The translation initiation codon was located within the third exon. Exon VIII encoded the COOH terminus of the CD20 protein and the long 3' untranslated region. Three forms of CD20 mRNA were identified that all encode an identical protein product. The dominant form of 2.8 kb results from usage of exons I through VIII, whereas a second form that is 263 bp shorter had exon I spliced into an internal 3' splice site within exon III thereby skipping exon II. A minor 3.4-kb mRNA species most likely results from an uncharacterized upstream exon(s) splicing into an internal 3' slice site located in exon I. Nucleotide sequences of cDNA clones representative of each of these RNA forms are presented. The 5' splice site following exon V was found to be divergent from the consensus splice sequence. A relationship between the individual peptides encoded by the six exons and structurally distinct regions of the CD20 protein is likely.

PMID: 2466899 [PubMed - indexed for MEDLINE]

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1: J Clin Oncol. 1998 Aug;16(8):2825-33.

Related Articles, Links

Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: half of patients respond to a four-dose treatment program.

McLaughlin P, Grillo-Lopez AJ, Link BK, Levy R, Czuczman MS, Williams ME, Heyman MR, Bence-Bruckler I, White CA, Cabanillas F, Jain V, Ho AD, Lister J, Wey K, Shen D, Dallaire BK.

Department of Hematology, University of Texas M.D. Anderson Cancer Center, Houston 77030, USA. pmclaugh@notes.mdacc.tmc.edu

PURPOSE: The CD20 antigen is expressed on more than 90% of B-cell lymphomas. It is appealing for targeted therapy, because it does not shed or modulate. A chimeric monoclonal antibody more effectively mediates host effector functions and is itself less immunogenic than are murine antibodies. PATIENTS AND METHODS: This was a multiinstitutional trial of the chimeric anti-CD20 antibody, IDEC-C2B8. Patients with relapsed low grade or follicular lymphoma received an outpatient treatment course of IDEC-C2B8 375 mg/m2 intravenously weekly for four doses. RESULTS: From 31 centers, 166 patients were entered. Of this intent-to-treat group, 48% responded. With a median follow-up duration of 11.8 months, the projected median time to progression for responders is 13.0 months. Serum antibody levels were sustained longer after the fourth infusion than after the first, and were higher in responders and in patients with lower tumor burden. The majority of adverse events occurred during the first infusion and were grade 1 or 2; fever and chills were the most common events. Only 12% of patients had grade 3 and 3% grade 4 toxicities. A human antichimeric antibody was detected in only one patient. CONCLUSION: The response rate of 48% with IDEC-C2B8 is comparable to results with single-agent cytotoxic chemotherapy. Toxicity was mild. Attention needs to be paid to the rate of antibody infusion, with titration according to toxicity. Further investigation of this agent is warranted, including its use in conjunction with standard chemotherapy.

Publication Types:

- Clinical Trial
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L6 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
2004:482032 Document No. 141:37605 Gene expression profile in activated human CD4+ T cells useful for the diagnosis and treatment of immune-related diseases. Clark, Hilary; Hunte, Bridsell; Jackman, Janet; Schoenfeld, Jill; Willians, Mickey P.; Wood, William I.; Wu, Thomas D.; Bodary, Sarah (Genentech, Inc., USA). PCT Int. Appl. WO 2004047728 A2 20040610, 8598 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-XA35971 20031124. PRIORITY: US 2002-PV429069 20021126; WO 2003-US35971 20031124.

AB The present invention relates to compns. containing novel proteins and methods of using those compns. for the diagnosis and treatment of immune-related diseases. Microarray anal. of human CD4+ T-cells activated with an anti-CD3 antibody together with either ICAM-1 or anti-CD28 antibody provides genes that are differentially expressed in comparison to resting CD4+ T-cells. [This abstract record is one of two records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L6 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
2004:203694 Document No. 140:252300 DNA vaccines encoding human or chimeric human interleukin 13 and **T cell epitopes** for treating asthma, COPD and atopic disorders. Ashman, Claire; Ellis, Jonathan Henry (Glaxo Group Limited, UK). PCT Int. Appl. WO 2004019974 A2 20040311, 89 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,

MD, RU; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB3703 20030828. PRIORITY: GB 2002-20212 20020830; GB 2003-4672 20030228.

AB The present invention relates to isolated immunogens and their use in the treatment of diseases that are treatable with neutralization of IL-13, such as COPD, asthma and atopic disorders such as hayfever, contact allergies and atopic dermatitis. In particular the invention relates to the neutralization of the biol. effects of IL-13 by raising an immune response against the IL-13 by vaccination of a mammal with immunogens comprising the native or mutated amino acid sequence of IL-13, and foreign T-helper epitopes either inserted in, or attached to the IL-13 sequence or present in carrier polypeptides. Also provided by the present invention are DNA vaccines that comprise a polynucleotide sequence that encodes the immunogens of the present invention. The invention further relates to pharmaceutical compns. comprising such immunogens and their use in medicine and to methods for their production

L6 ANSWER 3 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

2004:181439 Document No.: PREV200400181290. Gene therapy for tolerance to the C2 domain of factor VIII. Scott, David W. [Reprint Author]; Qian, Jiahua [Reprint Author]; Lei, Tie Chi [Reprint Author]. Dept. of Immunology, Holland Lab of the American Red Cross, Rockville, MD, USA. Blood, (November 16 2003) Vol. 102, No. 11, pp. 163a. print. Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology. CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB We have utilized a platform technology for tolerance in which we engineer retroviral constructs to drive expression (in B cells) of different antigens in frame at the N-terminus of a murine IgG1 heavy chain. Previously, we have shown that recipients of B-cell blasts, transduced with an Ig fusion of a variety of model antigens or autoimmune targets constructs, are tolerant to the protein epitopes of the expressed genes and that this therapy can lead to modulation of clinical disease (Agarwal, R. et al. J. Clin. Invest. 106: 245, 2000; Melo, M. et al. J. Immunol. 168: 4788, 2002). Importantly, tolerance is more effective and of longer duration in the presence of the IgG backbone (Kang Y. et al. PNAS 96: 8609, 1999). Tolerance requires MHC class II expression on the presenting (transduced) cells but does not involve **Fc** receptors (El-Amine et al. J. Immunol. 165: 5631, 2000 & Internat. Immunol. 14:761, 2002). Based on our identification of major **T-cell epitopes** in the C2 region of factor VIII (Pratt et al., submitted, 2003; http://www.abstracts-on-line.com/abstracts/hemphiladelphia02) and the fact that many "inhibitors" bind to an exposed region of C2, we have now inserted residues 2173-2332 of fVIII onto the IgG heavy chain carrier to induce tolerance in hemophilic mice. In the current study, we show that effective suppression of immunity can be achieved when lipopolysaccharide (LPS)-activated B-cell blasts are transduced with a fusion IgG containing this entire C2 domain and injected into naive recipients. Both the splenic T-cell proliferative response and primary IgG antibody to C2 epitopes are significantly reduced by this treatment. However, the responses to fVIII per se are only modestly affected, presumably due to recognition of non-C2 epitopes. It is not known yet whether inhibitor titers are reduced by C2-Ig B-cell therapy. Nonetheless, we are engineering a factor VIII A2 domain sequence (p379-740) into the Ig **fusion protein** for combined use with C2-Ig and increased therapeutic efficacy. Our results suggest that B cell presentation fVIII domains on an Ig backbone may be effective therapeutics for inhibitor formation.

L6 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

2002:778117 Document No. 137:293537 Reducing the immunogenicity of **fusion proteins.** Gillies, Stephen D. (Lexigen Pharmaceuticals Corp., USA). PCT Int. Appl. WO 2002079415 A2 20021010, 67 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,

BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US9650 20020329. PRIORITY: US 2001-PV280625 20010330.

AB Compns. and methods for producing **fusion proteins** with reduced immunogenicity are disclosed. **Fusion proteins** of the invention include a junction region having an amino acid change that reduces the ability of the neoepitope to bind to MHC Class II, thereby reducing its interaction with T-cells. In one example, reduced immunogenicity was observed for an interleukin-2 immunocytokine targeting EP-CAM wherein the C-terminal **Fc** region of the construct was engineered to eliminate a potential **T-cell epitope.**

L6 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

2002:658159 Document No. 137:200267 **Fusion proteins** comprising immunoglobulin and target antigen with reduced **T cell epitope** and immunogenicity for therapeutic use. Gillies, Stephen; Carr, Francis J.; Jones, Tim; Carter, Graham; Hamilton, Anita; Williams, Stephen; Hanlon, Marian; Watkins, John; Baker, Matthew; Way, Jeffrey C. (Merck Patent G.m.b.H., Germany). PCT Int. Appl. WO 2002066514 A2 20020829, 92 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP1690 20020218. PRIORITY: EP 2001-103955 20010219; EP 2001-108291 20010405.

AB The invention relates to artificial modified proteins, preferably **fusion proteins**, having a reduced immunogenicity compared to the parent non-modified mol. when exposed to a species in vivo. The invention relates, above all, to novel Ig **fusion proteins** which essentially consist of an Ig mol. or a fragment thereof covalently fused via its C-terminus to the N-terminus of a biol. active non-Ig mol., preferably a polypeptide or protein or a biol. active fragment thereof. In a specific embodiment, the invention relates to **fusion proteins** consisting of an **Fc** portion of an antibody which is fused as mentioned to the non-immunol. target mol. which elicits biol. or pharmacol. efficacy. The mols. of the invention have amino acid sequences which are altered in one or more amino acid residue positions but have in principal the same biol. activity as compared with the non-altered mols. The changes are made in regions of the mols. which are identified as **T-cell epitopes**, which contribute to an immune reaction in a living host. Thus, the invention also relates to a novel method of making such **fusion proteins** by identifying said epitopes comprising calcn. of **T-cell epitope** values for MHC Class II mol. binding sites in a peptide by computer-aided methods.

L6 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

2002:574952 Document No. 137:139357 Chimeric antibodies comprising CD64-binding human **Fc** and heterologous **T cell epitopes** for stimulating cytotoxic T cell response against pathogens and tumor. Durrant, Linda Gillian; Parsons, Tina; Robins, Adrian (Scancell Limited, UK; Cancer Research Campaign Technology Limited). PCT Int. Appl. WO 2002058728 A2 20020801, 87 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB354 20020128. PRIORITY: GB 2001-2145 20010126.

AB The invention relates to the use of a polypeptide which comprises (i) a first portion comprising the part of human **Fc** which binds to CD64, and (ii) a second portion comprising one or more heterologous **T cell epitopes** for stimulating cytotoxic and helper T cell response. The polypeptide may be an antibody which may be used to stimulate an cytotoxic T cell response against pathogens and tumor cells in patients in need of such treatment.

L6 ANSWER 7 OF 15 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
2002:341220 The Genuine Article (R) Number: 540DJ. Immunization with a recombinant adenovirus encoding a lymphoma idiotype: Induction of tumor-protective immunity and identification of an idiotype-specific **T cell epitope.** Armstrong A C; Dermime S; Allinson C G; Bhattacharyya T; Mulryan K; Gonzalez K R; Stern P L; Hawkins R E (Reprint). Christie Hosp NHS Trust, Paterson Inst Canc Res, Canc Res Campaign, Dept Med Oncol, Manchester M20 4BX, Lancs, England (Reprint); Christie Hosp NHS Trust, Paterson Inst Canc Res, Canc Res Campaign, Dept Immunol, Manchester M20 4BX, Lancs, England. JOURNAL OF IMMUNOLOGY (15 APR 2002) Vol. 168, No. 8, pp. 3983-3991. Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA. ISSN: 0022-1767. Pub. country: England. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The Ig Id of a B cell lymphoma is a tumor-specific Ag, although as a self-Ag it is likely to be a weak immunogen. Provision of a foreign gene may enhance the immunogenicity of the idiotype. Viral vectors allow highly efficient transfer of genetic material and are themselves innately immunogenic. We have investigated the ability of recombinant adenoviral vectors, encoding the idiotypic gene with or without fusion to the human **Fc** region, to produce anti-idiotypic Ab- and T cell-mediated responses in a syngeneic BALB/c A20 murine lymphoma model. The idiotypic V-H and V-L sequences were assembled as a single chain variable fragment (scFv) and adenoviral vectors encoding the A20 scFv (Ad.A20) and A20 scFv linked to the **Fc** fragment of human IgG1 (Ad.A20hFc) were constructed. A single immunization of BALB/c mice with Ad.A20hFc but not Ad.A20 induced a specific anti-idiotypic Ab response. T cell lines generated from mice vaccinated with either vector displayed specific cytotoxicity, proliferation, and IFN-gamma release against a syngeneic dendritic cell line transduced using a retroviral vector to express the A20 scFv idiotype (XS52.A1.A20). Importantly, both T cell lines lysed the A20 lymphoma cells. An immunodominant H-2K(d)-restricted CD8(+) T cell peptide, DYWGQGTEL (A20[106-114]), was identified as a naturally occurring A20 scFv epitope. A single immunization with Ad.A20hFc but not Ad.A20 provided protection in >40% of animals challenged with a lethal dose of the A20 tumor line and was more effective, in this model, than a previously optimized plasmid vaccine.

L6 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
2001:101190 Document No. 134:161885 Therapeutic compounds comprised of anti-**Fc** receptor binding agents. Deo, Yashwant M.; Goldstein, Joel; Graziano, Robert; Keler, Tibor (Medarex, Inc., USA). PCT Int. Appl. WO 2001009186 A2 20010208, 185 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO

'2000-US20158 20000725. PRIORITY: US 1999-364088 19990730; US 2000-523279 20000310.

AB Multispecific mols. which induce effector cell-mediated killing of target cells are disclosed. The mols. are "multispecific" because they bind to multiple (two or more), distinct targets, one of which is an **Fc** receptor on the surface of an immune cell. Multispecific mols. of the invention include mols. comprised of at least one portion which binds to an **Fc** receptor, such as an **Fc**<y receptor (e.g., **Fc**<yRI) or an **Fc**<a receptor, and at least one other portion which binds to a different target, such as an antigen on a tumor cell or a pathogen. Multispecific mols. of the invention also include antigen "multimer complexes" comprised of multiple (i.e., two or more) portions which bind to a mol. on an antigen presenting cell (APC), such as an **Fc** receptor, linked to one or more antigens. These multimer complexes target antigens, such as self-antigens, to APCs to induce and/or enhance internalization (endocytosis), processing and/or presentation of the antigen by the APC. Therefore, these mols. can be used to induce or enhance an immune response either in vivo or in vitro against a normally non-immunogenic protein, such as a self-antigen. In a particular embodiment, at least one portion of the multispecific mols. comprises a humanized or human antibody or antibody fragment (e.g., ScFv or Fab') which binds to an **Fc** receptor or a receptor on a target cell (e.g., EGF-R or HER2).

L6 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

1997:244373 Document No. 126:224282 Preparation of **fusion proteins** of allergens with monoclonal antibodies reactive with human **Fc**.gamma. receptor II (CD32) for treatment of allergies. Mudde, Geert C. (Sandoz Ltd., Switz.; Sandoz-Patent-Gmbh; Sandoz-Erfindungen Verwaltungsgesellschaft M.B.H.; Mudde, Geert C.). PCT Int. Appl. WO 9707218 A1 19970227, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-EP3616 19960816. PRIORITY: GB 1995-16760 19950816.

AB **Fusion proteins** are described comprising one or more antigens and one or more moieties interacting with human **Fc** γ receptor II (**Fc**.gamma.RII) (CD32). Thus, the major allergen I from Dermatophagoides pteronyssinus (or peptide fragments 101-143 or 101-131 containing the majority of **T-cell epitopes**) is fused to antibodies specific or CD32 (e.g., the Mc.a-CD32 monoclonal antibody, or its single-chain **Fc** derivative). Fusion is achieved by recombinant gene techniques to achieve a single contiguous amino acid sequence, or by covalent conjugation using a bifunctional coupling reagent such as SPDD. The aCD32-DerP1 construct stimulates the T-cell clone CFTS4:3.1 and inhibits IgE synthesis, and thus may be effective in prevention or treatment of allergies (including food allergies).

L6 ANSWER 10 OF 15 MEDLINE on STN DUPLICATE 2

1998098148. PubMed ID: 9435859. Increased potency of **Fc**-receptor-targeted antigens. Guyre P M; Graziano R F; Goldstein J; Wallace P K; Morganelli P M; Wardwell K; Howell A L. (Department of Physiology, Dartmouth-Hitchcock Medical Center, Lebanon, NH 03756, USA.. paul.guyre@dartmouth.edu) . Cancer immunology, immunotherapy : CII, (1997 Nov-Dec) 45 (3-4) 146-8. Ref: 13. Journal code: 8605732. ISSN: 0340-7004. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB A major challenge for using native and modified **T cell epitopes** to induce or suppress immunity relates to achieving efficient uptake and processing by antigen-presenting cells (APC) in vivo. IgG **Fc** receptors, which are expressed constitutively by professional APC including monocytes and dendritic cells, have long been

known to mediate antigen uptake in a manner leading to efficient T cell activation. We have previously demonstrated enhanced presentation of antigenic and antagonistic peptides by targeting them to the type I **Fc** receptor for IgG (**Fc** gamma RI, CD64) on human monocytes. In the present report we review the literature suggesting that CD64-targeted antigens are likely to be effective in vivo, and present data demonstrating enhanced immunogenicity in CD64 transgenic mice of a **fusion protein** that combines the specificities of HIV gp120 and the humanized anti-CD64 monoclonal antibody H22. Overall, these studies suggest that targeting antigens to CD64 represents an effective approach to enhancing the effectiveness of vaccines in vivo.

L6 ANSWER 11 OF 15 MEDLINE on STN DUPLICATE 3
96209851. PubMed ID: 8643522. Epitope-specific tolerance induction with an engineered immunoglobulin. Zambidis E T; Scott D W. (Department of Immunology, Holland Laboratory, American Red Cross, Rockville, MD 20855, USA.) Proceedings of the National Academy of Sciences of the United States of America, (1996 May 14) 93 (10) 5019-24. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB Isologous and heterologous immunoglobulins have been shown to be extremely effective as tolerogenic carriers for nearly 30 years. The efficacy of these proteins is due in part to their long half-life in vivo, as well as their ability to crosslink surface IgM with **Fc** receptors. The concept of using IgG as a carrier molecule to induce unresponsiveness in the adult immune system has been exploited for simple haptens, such as nucleosides, as well as for peptides. To further evaluate the in vivo potential of these molecules for inducing tolerance to a defined epitope, we have engineered a **fusion protein** of mouse IgG1 with the immunodominant epitope 12-26 from bacteriophage lambda cI repressor protein. This 15-mer, which contains both a B-cell and **T-cell epitope**, has been fused in-frame to the N terminus of a mouse heavy chain IgG1 construct, thus creating a "genetic hapten-carrier" system. We describe a novel in vitro and in vivo experimental system for studying the feasibility of engineered tolerogens, consisting of a recombinant flagellin challenge antigen and a murine IgG1 tolerogen, both expressing the lambda repressor epitope 12-26. Herein, we show that peptide-grafted IgG molecules injected i.v., or expressed by transfected, autologous B cells, can efficiently modulate the cellular and humoral immune responses to immunodominant epitopes. This model displays the feasibility of "tailor-designing" immune responses to whole antigens by selecting epitopes for either tolerance or immunity.

L6 ANSWER 12 OF 15 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
96:399880 The Genuine Article (R) Number: UK861. PRESENTATION OF AGONIST AND ANTAGONIST **T-CELL EPITOPES** TARGETED TO **FC**-GAMMA-RI ON HUMAN MONOCYTES USING ANTI-**FC**-GAMMA-RI ANTIBODY-BASED **FUSION PROTEINS.** LIU C (Reprint); GRAZIANO R F; GOLDSTEIN J; HE J; OSHEA J; GUYRE P M. DARTMOUTH COLL SCH MED, DEPT PHYSIOL, LEBANON, NH, 03756; MEDAREX INC, ANNANDALE, NJ, 08801. FASEB JOURNAL (30 APR 1996) Vol. 10, No. 6, pp. 2021. ISSN: 0892-6638. Pub. country: USA. Language: ENGLISH.

L6 ANSWER 13 OF 15 MEDLINE on STN DUPLICATE 4
97060283. PubMed ID: 8903318. F(c)gammaRI-targeted **fusion proteins** result in efficient presentation by human monocytes of antigenic and antagonist **T cell epitopes.** Liu C; Goldstein J; Graziano R F; He J; O'Shea J K; Deo Y; Guyre P M. (Department of Physiology, Dartmouth Medical School, Lebanon, New Hampshire 03756, USA.) Journal of clinical investigation, (1996 Nov 1) 98 (9) 2001-7. Journal code: 7802877. ISSN: 0021-9738. Pub. country: United States. Language: English.

AB A major challenge for using native or modified **T cell epitopes** to induce or suppress immunity relates to poor localization of peptides to antigen presenting cells (APCs) in vivo. In this study, we demonstrate enhanced presentation of antigenic and

antagonistic peptides by targeting them to the type I **Fc** receptor for IgG (F(c)gammaRI, CD64) on human monocytes. A Th epitope of tetanus toxoid, TT830, and the antagonistic peptide for TT830, TT833S, were genetically grafted into the constant region of the heavy chain of the humanized anti-CD64 mAb 22 and expressed as monovalent **fusion proteins**, Fab22-TT830 and Fab22-TT833S. These CD64-targeted peptides were up to 1,000- and 100-fold more efficient than the parent peptides for T cell stimulation and antagonism, respectively, suggesting that such **fusion proteins** could effectively increase the delivery of peptides to APCs in vivo. Moreover, the F(c)gammaRI-targeted antagonistic peptide inhibited proliferation of TT830-specific T cells even when APCs were first pulsed with native peptide, a situation comparable with that which would be encountered in vivo when attempting to ameliorate an autoimmune response. These data suggest that targeted presentation of antagonistic peptides could lead to promising Ag-specific therapies for T cell-mediated autoimmune diseases.

L6 ANSWER 14 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1996:310083 Document No.: PREV199699032439. Presentation of agonist and antagonist **T cell epitopes** targeted to **Fc**-gamma-RI on human monocytes using anti-**Fc**-gamma-RI antibody-based **fusion proteins.** Liu, C.; Graziano, R. F.; Goldstein, J.; He., J.; O'Shea, J.; Guyre, P. M.. Physiol. Dep., Dartmouth Med. Sch., Lebanon, NJ 03756, USA. FASEB Journal, (1996) Vol. 10, No. 6, pp. A1455.
Meeting Info.: Joint Meeting of the American Society for Biochemistry and Molecular Biology, the American Society for Investigative Pathology and the American Association of Immunologists. New Orleans, Louisiana, USA. June 2-6, 1996.
CODEN: FAJOEC. ISSN: 0892-6638. Language: English.

L6 ANSWER 15 OF 15 MEDLINE on STN
93134380. PubMed ID: 7678469. Presentation of a viral **T cell epitope** expressed in the CDR3 region of a self immunoglobulin molecule. Zaghouani H; Steinman R; Nonacs R; Shah H; Gerhard W; Bona C. (Department of Microbiology, Mount Sinai School of Medicine, New York, NY 10029.) Science, (1993 Jan 8) 259 (5092) 224-7. Journal code: 0404511. ISSN: 0036-8075. Pub. country: United States. Language: English.
AB Synthetic peptides corresponding to microbial epitopes stimulate T cell immunity but their immunogenicity is poor and their half-lives are short. A viral epitope inserted into the complementarity-determining region 3 (CDR3) loop of the heavy chain of a self immunoglobulin (Ig) molecule was generated from the Ig context and was presented by I-Ed class II molecules to virus-specific, CD4+ T cells. Chimeric Ig-peptide was presented 100 to 1000 times more efficiently than free synthetic peptide and was able to prime virus-specific T cells in vivo. These features suggest that antigenized Ig can provide an improved and safe vaccine for the presentation of microbial and other peptides.

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=> s CD20-Fc
L7          20 CD20-FC

=> dup remove l7
PROCESSING COMPLETED FOR L7
L8           9 DUP REMOVE L7 (11 DUPLICATES REMOVED)

=> d 18 1-9 cbib abs

L8   ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
2003:176760   Document No. 138:270192  The relationship of FcγRIIIa
     genotype to degree of B cell depletion by rituximab in the treatment of
     systemic lupus erythematosus.  Anolik, Jennifer H.; Campbell, Debbie;
     Felgar, Raymond E.; Young, Faith; Sanz, Inaki; Rosenblatt, Joseph; Looney,
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R. John (University of Rochester School of Medicine and Dentistry, Rochester, NY, USA). Arthritis & Rheumatism, 48(2), 455-459 (English) 2003. CODEN: ARHEAW. ISSN: 0004-3591. Publisher: John Wiley & Sons, Inc..

AB Objective: Despite wide use of the anti-CD20 monoclonal antibody rituximab in the treatment of B cell lymphomas, the mechanism by which it causes B cell depletion remains a subject of controversy. As part of an ongoing phase I/II trial of rituximab in the treatment of systemic lupus erythematosus (SLE), the authors sought to determine whether the effectiveness of B cell depletion was influenced by polymorphisms of Fc receptors (FcR) on effector cells. Methods: During rituximab treatment of 12 SLE patients, B cell depletion was monitored as a function of the serum rituximab level and FcγRIIa and FcγRIIIa genotypes at baseline and at 1 mo and 2 mo after treatment. FcR genotypes were determined by polymerase chain reaction. Serum levels of rituximab were measured by ELISA. B lymphocyte percentages were assessed by flow cytometry. Results: B cell depletion was highly variable in this patient cohort, with B cell percentages at the 1-2-mo posttreatment nadir ranging from undetectable (<0.1 cell/μl) to 16% (.apprx.30 cells/μl) of the total peripheral blood lymphocytes. At 2 mo posttreatment, B cell percentages were highly correlated with both the serum rituximab level and the FcγRIIIa genotype (R2 = 0.75). The FcγRIIIa genotype was a significant independent predictor of the efficacy of B cell depletion. Conclusion: These results highlight the potential variability of B cell depletion by rituximab in the treatment of autoimmune disease and indicate that Fc receptors are an important determinant of that variability. The findings further suggest the importance of antibody-dependent cell-mediated cytotoxicity and/or apoptosis induction via FcγRIIIa-expressing effector cells in the mechanism of B cell depletion by this widely used monoclonal antibody.

L8 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN

2002:615778 Document No. 137:164742 Human and murine MS4A gene family members expressed by hematopoietic cells. Tedder, Thomas F.; Liang, Ying Hua (Duke University, USA). PCT Int. Appl. WO 2002062946 A2 20020815, 450 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US48437 20011210. PRIORITY: US 2000-PV254362 20001208; US 2001-PV270057 20010220.

AB The invention provides 19 nucleic acids encoding MS4A family (membrane spanning 4-domain family, subfamily A) polypeptides expressed in human, mouse and pig that span the cell membrane at least four times and share high levels of amino acid sequence identity with **CD20**, **Fc**.epsilon.RIβ, and HTm4. Complete coding regions are predicted using overlapping nucleotide sequences obtained from sequenced ESTs and cDNAs that corresponded to unique, near full-length transcripts in human and mice. Human BACs containing MS4A genes are identified, and 3 putative genes encoding unique MS4A family members are localized to the q12-13.1 region of human chromosome 11. Splice variants and polymorphisms are also identified. Northern anal. and PCR amplification, indicate that most MS4A family members are expressed by hematopoietic cells (e.g., B cells), although the patterns of expression of each gene is distinct. The disclosed MS4A nucleic acids and polypeptides can be used to generate a mouse model of atopic disorders, for drug discovery screens, and for therapeutic treatment of atopic disorders or other MS4A-related conditions.

L8 ANSWER 3 OF 9 MEDLINE on STN DUPLICATE 1

2002140847. PubMed ID: 11841845. Down regulation of B cells by

immunization with a fusion protein of a self CD20 peptide and a foreign IgG.Fc fragment. Huang Janice; Sheu Jim Jinn Chyuan; Wu Stanley Chi Shen; Chang Tse Wen. (College of Life Science, National Tsing Hua University, Hsinchu, Taiwan, ROC.) Immunology letters, (2002 Apr 1) 81 (1) 49-58. Journal code: 7910006. ISSN: 0165-2478. Pub. country: Netherlands. Language: English.

AB In vivo studies of mice were performed to investigate whether auto-reactive antibodies specific for self CD20 antigen on B cells could be induced by immunizing with a CD20 peptide linked to a foreign, human IgG.Fc fragment through a T cell immunologically inert linker peptide and how such an auto-reactivity, if generated, would affect the levels of B cells. The dimeric Fc fusion protein containing the extracellular 44-amino acid portion of CD20, and the CH2-CH3 domains of human gamma 1 immunoglobulin were prepared. After several subcutaneous immunizations with this **CD20-Fc** protein, mice produced anti-CD20 antibodies that can bind to native CD20 on normal B cells and B-lymphoma cells. In mice immunized with the **CD20-Fc** protein, the fraction of B cells in total peripheral blood lymphocytes decreased to about 40%, significantly lower than that of mice immunized with human IgG. In addition, antibody response towards an irrelevant bystander antigen, chicken ovalbumin, was weakened compared with that of mice immunized with human IgG. These results show that auto-reactive antibodies specific for CD20 can be induced by immunizing with an autologous CD20 peptide fused with a foreign IgG.Fc and that the auto-antibodies can partially reduce the levels of B cells and their response to other antigens.

L8 ANSWER 4 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

2001:260645 The Genuine Article (R) Number: 410KA. Identification of a **CD20**, **Fc** epsilon R1 beta and HTm4 related gene family: Sixteen new MS4A family members expressed in human and mouse. Liang Y H (Reprint); Tedder T F. Duke Univ, Med Ctr, Dept Immunol, Durham, NC 27710 USA. FASEB JOURNAL (7 MAR 2001) Vol. 15, No. 4, Part 1, pp. A713-A713. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA. ISSN: 0892-6638. Pub. country: USA. Language: English.

L8 ANSWER 5 OF 9 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 2

2001342646 EMBASE CFFM4: A new member of the **CD20/Fc** εRIβ family. Gingras M.-C.; Lapillonne H.; Margolin J.F..

M.-C. Gingras, Baylor College of Medicine, Texas Children's Cancer Center, Texas Children Hospital, 6621 Fannin Street, Houston, TX 77030, United States. mgingras@txccc.org. Immunogenetics 53/6 (468-476) 2001.

Refs: 34.

ISSN: 0093-7711. CODEN: IMNGBK. Pub. Country: Germany. Language: English. Summary Language: English.

AB Proteins with transmembrane domains are classified in different families based on their structure, amino acid homology, and function. In this study, we report the identification, sequence, and expression profile of a new member of the **CD20/Fc**.epsilon.RIβ family, **CD20/Fc**.epsilon.RIβ family member 4 (CFFM4). The CFFM4 gene contains seven exons and six introns and is transcribed into an mRNA encoding a 240-amino acid protein with four hydrophobic regions. The CFFM4 protein shares a high degree of homology with the other members of the family, especially in the hydrophobic regions where several amino acids are conserved. However, the CFFM4 protein can be distinguished from the other members of the family based on the length of the second extracellular loop and the absence of an immunoreceptor tyrosine-based activation motif signal. Another distinct characteristic is that CFFM4 mRNA expression is not limited to the hematopoietic lineage. CFFM4 was detected by Northern dot blot in a variety of normal and cancerous tissues. CFFM4 expression was also compared in developmentally early hematopoietic human bone marrow CD34(+) stem cells versus peripheral blood-derived CD14(+) mature monocytes, in the undifferentiated versus differentiated myelomonocytic U937 cell line, and in acute myelogenous leukemia FAB1 versus FAB5. In each of these systems, cellular

myelomonocytic differentiation correlated with an increase in CFFM4 mRNA expression. Such results indicate that CFFM4 is associated with mature cellular function in the monocytic lineage and like CD20 and FcεRIβ, it may be a component of a receptor complex involved in signal transduction.

L8 ANSWER 6 OF 9 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 3

2001347701 EMBASE Isolation, tissue distribution, and chromosomal localization of a novel testis-specific human four-transmembrane gene related to CD20 and FcεRI-β. Hulett M.D.; Pagler E.; Hornby J.R.; Hogarth P.M.; Eyre H.J.; Baker E.; Crawford J.; Sutherland G.R.; Ohms S.J.; Parish C.R.. M.D. Hulett, Division of Immunology, John Curtin Sch. of Medical Research, ANU, P.O. Box 334, Canberra, ACT 2601, Australia. mark.hulett@anu.edu.au. Biochemical and Biophysical Research Communications 280/1 (374-379) 2001.
Refs: 12.
ISSN: 0006-291X. CODEN: BBRCA. Pub. Country: United States. Language: English. Summary Language: English.

AB CD20 and the β subunit of the high affinity receptor for IgE (FcεRIβ) are related four-transmembrane molecules that are expressed on the surface of hematopoietic cells and play crucial roles in signal transduction. Herein, we report the identification and characterization of a human gene, TETM4, that encodes a novel four-transmembrane protein related to CD20 and FcεRIβ. The predicted TETM4 protein is 200 amino acids and contains four putative transmembrane regions, N- and C-terminal cytoplasmic domains, and three inter-transmembrane loop regions. TETM4 shows 31.0 and 23.2% overall identity with CD20 and FcεRIβ respectively, with the highest identity in the transmembrane regions, whereas the N- and C-termini and inter-transmembrane loops are more divergent. Northern blot and RT-PCR analysis suggest that TETM4 mRNA has a highly restricted tissue distribution, being expressed selectively in the testis. Using fluorescence in situ hybridization and radiation hybrid analysis, the TETM4 gene has been localized to chromosome 11q12. The genes for CD20 and FcεRIβ have also been mapped to the same region of chromosome 11 (11q12-13.1), suggesting that these genes have evolved by duplication to form a family of four-transmembrane genes. TETM4 is the first nonhematopoietic member of the **CD20/Fc** εRIβ family, and like its hematopoietic-specific relatives, it may be involved in signal transduction as a component of a multimeric receptor complex. .COPYRGT. 2001 Academic Press.

L8 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN

2001:566542 Document No. 136:380871 Structural organization of the human MS4A gene cluster on Chromosome 11q12. Liang, Yinghua; Buckley, Thomas R.; Tu, LiLi; Langdon, Scott D.; Tedder, Thomas F. (Department of Immunology, Duke University Medical Center, Durham, NC, 27710, USA). Immunogenetics, 53(5), 357-368 (English) 2001. CODEN: IMNGBK. ISSN: 0093-7711. Publisher: Springer-Verlag.

AB CD20, the high-affinity IgE receptor β chain (FcεRIβ), and HTm4 are structurally related cell surface proteins expressed by hematopoietic cells. Recently, 16 novel human and mouse genes were identified that encode new members of this nascent protein family that we have named the membrane-spanning 4A gene family, with at least 12 subgroups (MS4A1-MS4A12). In the current study, we identified three addnl. human MS4A genes:MS4A4E, MS4A6E, and MS4A10. All family members have at least four potential transmembrane domains and N- and C-terminal cytoplasmic domains encoded by distinct exons, except MS4A6E which contains two transmembrane domains. Otherwise, the 12 currently identified MS4A genes share common structural features and similar intron/exon splice boundaries, and are clustered along an .apprx.600-kb region of Chromosome 11q12. In contrast to other MS4A genes, MS4A4E, MS4A6E, and MS4A10 transcripts were rare and not detected among hematopoietic cells and most nonlymphoid tissues. Sequence polymorphisms

were identified in the MS4A6E gene and common splice variants were observed for the MS4A4A, MS4A5 ,MS4A6A, and MS4A7 genes. Thus, the MS4A family currently includes 24 distinct human and mouse genes. Like CD20 and FcεRIβ, the 10 other human MS4A family members are likely to be components of oligomeric cell surface complexes involved in signal transduction in diverse cell lineages.

L8 ANSWER 8 OF 9 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 4
2001119535 EMBASE Identification of a **CD20**-, **Fc**
εRIβ-, and HTm4-related gene family: Sixteen new MS4A family members expressed in human and mouse. Liang Y.; Tedder T.F.. T.F. Tedder, Department of Immunology, Box 3010, Duke University Medical Center, Research Drive, Durham, NC 27710, United States. thomas.tedder@duke.edu.
Genomics 72/2 (119-127) 1 Mar 2001.
Refs: 33.
ISSN: 0888-7543. CODEN: GNMCEP. Pub. Country: United States. Language: English. Summary Language: English.
AB CD20, high-affinity IgE receptor β chain (FcεRIβ), and HTm4 are structurally related cell-surface proteins expressed by hematopoietic cells. In the current study, 16 novel human and mouse genes that encode new members of this nascent protein family were identified. All family members had at least four potential membrane-spanning domains, with N- and C-terminal cytoplasmic domains. This family was therefore named the membrane-spanning 4A gene family, with at least 12 subgroups (MS4A1 through MS4A12) currently representing at least 21 distinct human and mouse proteins. Each family member had unique patterns of expression among hematopoietic cells and nonlymphoid tissues. Four of the 6 human MS4A genes identified in this study mapped to chromosome 11q12q13.1 along with **CD20**, **Fc**.epsilon.RIβ, and HTm4. Thus, like CD20 and FcεRIβ, the other MS4A family members are likely to be components of oligomeric cell surface complexes that serve diverse signal transduction functions. .COPYRGT. 2001 Academic Press.

L8 ANSWER 9 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
1999:1226 The Genuine Article (R) Number: 141AW. Gene structure, sequence, fine expression analysis and cellular localization of HTm4, a **CD20** /**Fc** epsilon RI beta homologue and a candidate gene for atopy..
Adra C N (Reprint); Iyengar A R; Syed F A; Donato J L; Lin S R; Hu W; Cheng T; Scadden D T; Shirakawa T; Lim B. UNIV OXFORD, OXFORD OX1 2JD, ENGLAND; HARVARD UNIV, MASSACHUSETTS GEN HOSP, SCH MED, BETH ISRAEL DEACONESS MED CTR, BOSTON, MA. BLOOD (15 NOV 1998) Vol. 92, No. 10, Part 1, Supp. [1], pp. 658-658. Publisher: W B SAUNDERS CO. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0006-4971.
Pub. country: ENGLAND; USA. Language: English.

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=> s CD20 fusion protein
L9          12 CD20 FUSION PROTEIN

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10          6 DUP REMOVE L9 (6 DUPLICATES REMOVED)

=> d l10 1-6 cbib abs
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L10 ANSWER 1 OF 6 MEDLINE on STN DUPLICATE 1
2004305043. PubMed ID: 14996706. Phase 1 trial of a novel anti-**CD20 fusion protein** in pretargeted radioimmunotherapy for B-cell non-Hodgkin lymphoma. Forero Andres; Weiden Paul L; Vose Julie M; Knox Susan J; LoBuglio Albert F; Hankins Jordan; Goris Michael L; Picozzi Vincent J; Axworthy Don B; Breitz Hazel B; Sims Robert B; Ghalie Richard G; Shen Sui; Meredith Ruby F. (University of Alabama at Birmingham Comprehensive Cancer Center, 35294-3300, USA.. andres.forero@ccc.uab.edu) . Blood, (2004 Jul 1) 104 (1) 227-36. Journal

code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB Pretargeted radioimmunotherapy (PRIT) has the potential to increase the dose of radionuclide delivered to tumors while limiting radiation to normal tissues. The purpose of this phase 1 trial is to assess safety of this multistep approach using a novel tetrameric single-chain anti-CD20-streptavidin fusion protein (B9E9FP) as the targeting moiety in patients with B-cell non-Hodgkin lymphoma (NHL), and to characterize its pharmacokinetics and immunogenicity. All patients received B9E9FP (160 mg/m(2) or 320 mg/m(2)); either 48 or 72 hours later, a synthetic clearing agent (sCA) was administered (45 mg/m(2)) to remove circulating unbound B9E9FP. (90)Yttrium ((90)Y; 15 mCi/m(2))/(111)In (5 mCi)-DOTA-biotin was injected 24 hours later. There were 15 patients enrolled in the study. B9E9FP had a mean plasma half-life (T(1/2)) of 25 +/- 6 hours with a reduction in plasma level of more than 95% within 6 hours of sCA administration. (90)Y/(111)In-DOTA-biotin infusion resulted in rapid tumor localization and urinary excretion. The ratio of average tumor to whole-body radiation dose was 49:1. No significant hematologic toxicities were noted in 12 patients. There were 2 patients who had hematologic toxicity related to progressive disease. There were 2 complete remissions (90 and 325 days) and one partial response (297 days). B9E9FP performs well as the targeting component of PRIT with encouraging dosimetry, safety, and efficacy. A dose escalation trial of (90)Y-DOTA-biotin in this format is warranted.

L10 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

2003:971282 Document No. 140:26899 Method and compositions for stimulation of an immune response to CD20 using a xenogeneic CD20 antigen. Palomba, Maria Lia; Houghton, Alan; Wolchok, Jedd; Scheinberg, David A.; Roberts, Wendy K. (USA). U.S. Pat. Appl. Publ. US 2003228326 A1 20031211, 17 pp., Cont.-in-part of U.S. Ser. No. 627,694. (English). CODEN: USXXCO. APPLICATION: US 2002-285874 20021031. PRIORITY: US 1997-308697 19970217; US 1997-PV36419 19970218; WO 1997-US22669 19971210; US 2000-627694 20000728.

AB Tolerance of the immune system for endogenous CD20 can be overcome and an immune response stimulated by administration of xenogeneic or xenoexpressed CD20 antigen. For example, mouse CD20, or antigenically-effective portions thereof, can be used to stimulate an immune response to the corresponding differentiation antigen in a human subject. Administration of xenogeneic antigens in accordance with the invention results in an effective immunity against CD20 expressed by the cancer in the treated individual, thus providing a therapeutic approach to the treatment of lymphomas and leukemia expressing CD20. For production of a recombinant mouse **CD20 fusion protein** (recCD20) the inventors used the baculovirus expression system to obtain a partially purified recCD20 for the use as xenoexpressed CD20.

L10 ANSWER 3 OF 6 MEDLINE on STN DUPLICATE 2

2003064199. PubMed ID: 12573619. An oncolytic measles virus engineered to enter cells through the CD20 antigen. Bucheit Amanda D; Kumar Shaji; Grote Deanna M; Lin Yukang; von Messling Veronika; Cattaneo Roberto B; Fielding Adele K. (Mayo Clinic Molecular Medicine Program, 200 First Street SW, Rochester, Minnesota 55902, USA.) Molecular therapy : journal of the American Society of Gene Therapy, (2003 Jan) 7 (1) 62-72. Journal code: 100890581. ISSN: 1525-0016. Pub. country: United States. Language: English.

AB We have earlier shown that attenuated measles virus (MV) has therapeutic potential as a replicating oncolytic virus in models of non-Hodgkin's lymphoma (NHL). In the current study, we investigated whether we could obtain replicating MVs capable of entering CD20(+) target cells through an interaction between a single-chain (scFv) anti-CD20 antibody and the CD20 antigen, a target of considerable clinical relevance in NHL. We replaced the H envelope glycoprotein of MV by an H-scFv anti-**CD20 fusion protein** with and without a protease-cleavable linker. Biochemical analysis of purified virions confirmed that the

modified H proteins were incorporated into the viral particles with efficiency similar to unmodified H. Experiments employing CHO cells and CHO cells expressing human CD20 indicated that the MVH alpha CD20 viruses were able to replicate well in CHOCD20 but not CHO cells. MVH alpha CD20 or a nonmodified control MV were administered systemically to immunodeficient mice bearing bilateral human tumor xenografts, one side with and the other side without CD20 expression. Growth of CD20(+) tumors was retarded by MVH alpha CD20 as compared with the control virus. The viruses had equivalent effects on the CD20(-) tumors. Thus we have demonstrated that the entry of a replicating oncolytic virus can be mediated through an interaction between a highly clinically relevant single-chain antibody and its target antigen, and we have shown that this interaction enhances in vivo oncolytic activity.

L10 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2003:584236 Document No.: PREV200300583962. The use of novel fusion proteins as targeting molecules in Pretarget(R) radioimmunotherapy (RIT). Forero-Torres, Andres [Reprint Author]; Meredith, Ruby F. [Reprint Author]; Knox, Susan J.; Vose, Julie M.; Picozzi, Vincent J.; Shen, Sui [Reprint Author]; Breitz, Hazel; Sims, Robert B.; LoBuglio, Albert F. [Reprint Author]. University of Alabama at Birmingham, Birmingham, AL, USA. Human Antibodies, (2003) Vol. 12, No. 1-2, pp. 9. print.
Meeting Info.: Tenth International Conference on Human Antibodies & Hybridomas. Osaka, Japan. October 08-10, 2003.
'ISSN: 1093-2607. Language: English.

L10 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3
2002:455929 Document No.: PREV200200455929. Pretarget radioimmunotherapy (RIT) with anti-**CD20 fusion protein** in patients with non-Hodgkin's lymphoma (NHL). Meredith, R. [Reprint author]; Shen, S.; Breitz, H.; Fisher, D.; Goris, M.; Knox, S.; Hankins, J.; Vose, J.; Picozzi, V.. University of Alabama, Birmingham, AL, USA. Journal of Nuclear Medicine, (May, 2002) Vol. 43, No. 5 Supplement, pp. 116P-117P. print.
Meeting Info.: 49th Annual Meeting of the Society of Nuclear Medicine. Los Angeles, CA, USA. June 15-19, 2002.
CODEN: JNMEAQ. ISSN: 0161-5505. Language: English.

L10 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2002:157379 Document No. 136:293206 Multimerization of a chimeric anti-CD20 single-chain Fv-Fc fusion protein is mediated through variable domain exchange. Wu, Anna M.; Tan, Giselle J.; Sherman, Mark A.; Clarke, Patrick; Olafsen, Tove; Forman, Stephen J.; Raubitschek, Andrew A. (Dep. of Mol. Biol., Beckman Res. Inst. of the City of Hope, Duarte, CA, 91010, USA). Protein Engineering, 14(12), 1025-1033 (English) 2001. CODEN: PRENE9. ISSN: 0269-2139. Publisher: Oxford University Press.
AB A series of single-chain anti-CD20 antibodies was produced by fusing single-chain Fv (scFv) with human IgG1 hinge and Fc regions, designated ,scFv-Fc. The anti-CD20 scFv-Fc retained its specific binding to CD20-pos. cells and was active in mediating complement-dependent cytolysis. However, the purified scFv-Fc included multimeric as well as monomeric components as revealed in the size-exclusion HPLC anal. Variant scFv-Fc were constructed incorporating four different hinges between the scFv and Fc regions, or three different linkers in the scFv domain. All formed multimers, with the highest level of multimerization observed in the scFv-Fc with the shortest linker (8 aa). The structural anal. of the scFv-Fc constructed with 18 or 8 aa linkers by pepsin or papain cleavage indicated that the proteins contained a form in which scFv units had cross-paired to form a "diabody". Such a domain exchange or cross-pairing appears to be the basis of the observed multimerization.

=> s CD20 conjugate
L11 1 CD20 CONJUGATE

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=> d '111 cbib abs

L11  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
2000:628370  Document No. 133:221570  Radiolabeling kit and binding assay.
     Chinn, Paul; Morena, Ronald; Labarre, Michael; Leonard, John E. (Idec
     Pharmaceuticals Corp., USA).  PCT Int. Appl. WO 2000052473 A2 20000908,
     231 pp.  DESIGNATED STATES: W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR,
     BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM,
     HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
     LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
     SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG,
     KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK,
     ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD,
     TG.  (English).  CODEN: PIXXD2.  APPLICATION: WO 2000-US5061 20000229.
     PRIORITY: US 1999-259337 19990301.
AB   Antibody binding assays and radiolabeling kits are disclosed for
     radiolabeling and testing therapeutic antibodies in the com. setting.  In
     particular, the kits are designed for making and evaluating radiolabeled
     anti-CD20 conjugates to be used for the treatment and
     imaging of B cell lymphoma tumors.  All kit reagents are sterile and are
     designed to achieve a high level of antibody radiolabeling and product
     stability with results which are highly reproducible.


=> s CD79 fusion
L12           1 CD79 FUSION

=> d l12 cbib abs


L12  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
2000:756855  Document No. 133:318803  Synthetic signal transducing proteins
     using motifs associated with receptor binding and activation.  Lawson,
     Alastair David Griffiths; Finney, Helene Margaret (Celltech Therapeutics
     Limited, UK).  PCT Int. Appl. WO 2000063372 A1 20001026, 74 pp.
     DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA,
     CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
     HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
     MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
     SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG,
     KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK,
     ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD,
     TG.  (English).  CODEN: PIXXD2.  APPLICATION: WO 2000-GB1456 20000417.
     PRIORITY: GB 1999-8807 19990416.
AB   The invention relates to synthetic signalling mols., which are based on
     sequences derived from primary signalling motifs such as Ig tyrosine
     receptor-based activation motifs (ITAMs).  The use of such signalling
     mols. within chimeric receptor proteins allows one to tailor the level of
     intracellular signalling mediated by the chimeric receptor.  Proteins
     containing, and nucleic acids encoding, such synthetic signalling mols.
     suitable for use in medicine, are described.


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=> s CD79 chimeric protein
L13           0 CD79 CHIMERIC PROTEIN

=> s CD79 conjugate
L14           0 CD79 CONJUGATE

=> s CD79
L15         301 CD79
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=> s l15 and fusion
L16             7 L15 AND FUSION

=> s l16 and Fc
L17             0 L16 AND FC

=> dup remove l16
PROCESSING COMPLETED FOR L16
L18             7 DUP REMOVE L16 (0 DUPLICATES REMOVED)

=> d l18 1-7 cbib abs

L18  ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2004 ACS on STN
2004:41226  Document No. 140:105321  Methods and compositions relating to
     isoleucine boroproline compounds.  Adams, Sharlene; Miller, Glenn T.;
     Jesson, Michael I.; Jones, Barry (Point Therapeutics, Inc., USA).  PCT
     Int. Appl. WO 2004004658 A2 20040115, 152 pp.  DESIGNATED STATES: W:  AE,
     AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
     CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
     IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG,
     MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
     SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZW,
     AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI,
     CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL,
     PT, SE, SN, TD, TG, TR.  (English).  CODEN: PIXXD2.  APPLICATION: WO
     2003-US21405 20030709.  PRIORITY: US 2002-PV394856 20020709; US
     2002-PV414978 20021001; US 2003-PV466435 20030428.
AB   A method for treating subjects with, inter alia, abnormal cell
     proliferation or infectious disease using agents of formula (I,
     AmNHCH(CH(CH3)CH2CH3)COA1R) (where Am and A1 are amino acids and R =
     organo boronates, organo phosphonates, fluoroalkyl ketones, alphaketos,
     N-peptiolyl-O-(acylhydroxylamines), azapeptides, azetidines, fluoroolefins
     dipeptide isosteres, peptidyl (α-aminoalkyl) phosphonate esters,
     aminoacyl pyrrolidine-2-nitriles and 4-cyanothiazolidides) is claimed.
     Methods for stimulating an immune response using the compds. of the
     invention are also claimed.  Compns. containing Ile-boroPro compds. are also
     provided as are kits containing the compns.  The invention embraces the use of
     these compds. alone or in combination with other therapeutic agents.

L18  ANSWER 2 OF 7  CAPLUS  COPYRIGHT 2004 ACS on STN
2003:417584  Document No. 139:5639  Anti-CD30 antibody-cytotoxic agent
     conjugates for treating non-cancer immunological disorders.  Law,
     Che-Leung; Klussman, Kerry; Wahl, Alan F.; Senter, Peter; Doronina,
     Svetlana; Toki, Brian (Seattle Genetics, Inc., USA).  PCT Int. Appl. WO
     2003043583 A2 20030530, 194 pp.  DESIGNATED STATES: W:  AE, AG, AL, AM,
     AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK,
     DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
     KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
     MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
     TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,
     MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES,
     FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG,
     TR.  (English).  CODEN: PIXXD2.  APPLICATION: WO 2002-US37223 20021120.
     PRIORITY: US 2001-PV331750 20011120.
AB   The present invention relates to methods for the treatment of immunol.
     disorders other than cancer, comprising administering proteins
     characterized by their ability to bind to CD30 and exert a cytostatic or
     cytotoxic effect on an activated lymphocyte.  Such proteins include
     monoclonal antibodies AC10 and HeFi1, AC10 and HeFi-1 derivs., and
     antibodies that compete with AC10 and HeFi-1 for binding to CD30.  Other
     such proteins include multivalent anti-CD30 antibodies and anti-CD30
     antibodies conjugated to cytotoxic agents.  These antibody conjugates are
     used for treating immunol. disorders such as autoimmune diseases,
     allergies, chronic inflammatory rections and graft vs. host diseases.
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L18 ANSWER 3 OF 7 MEDLINE on STN
2002645523. PubMed ID: 12384401. The alternative transcript of CD79b is overexpressed in B-CLL and inhibits signaling for apoptosis. Cragg Mark S; Chan H T Claude; Fox Mathew D; Tutt Alison; Smith Aimee; Oscier David G; Hamblin Terry J; Glennie Martin J. (Tenovus Research Laboratory, Cancer Sciences Division, University of Southampton School of Medicine, Southampton General Hospital, Tremona Road, Southampton SO16 6YD, UK.. msc@soton.ac.uk) . Blood, (2002 Nov 1) 100 (9) 3068-76. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB The B-cell receptor (BCR) for antigen is composed of surface immunoglobulin (sIg), which provides antigen specificity, and a noncovalently associated signaling unit, the CD79a/b heterodimer. Defects in **CD79** can influence both BCR expression and signaling and may explain why cells from certain malignancies, such as B-chronic lymphocytic leukemia (B-CLL), often express diminished and inactive BCR. Recently, an alternative transcript of CD79b (DeltaCD79b) has been reported that is up-regulated in B-CLL and may explain this diminished BCR expression. Here we assess the expression of DeltaCD79b in B-CLL and other lymphoid malignancies and investigate its function. High relative expression of DeltaCD79b was confirmed in most cases of B-CLL and found in 6 of 6 cases of splenic lymphomas with villous lymphocytes (SLVLs) and hairy cell leukemia. In a range of Burkitt lymphoma cell lines, expression of DeltaCD79b was relatively low but correlated inversely with the ability of the BCR to signal apoptosis when cross-linked by antibody (Ab). Interestingly, when Ramos-EHRB cells, which express low DeltaCD79b, were transfected with this transcript, they were transformed from being sensitive to anti-Fcmu-induced apoptosis to being highly resistant. Although DeltaCD79b was expressed as protein, its overexpression did not reduce the level of cell surface BCR. Finally, we showed that the inhibitory activity of DeltaCD79b depended on an intact leader sequence to ensure endoplasmic reticulum (ER) trafficking and a functional signaling immunoreceptor tyrosine-based activation motif (ITAM) in its cytoplasmic tail. These results point to DeltaCD79b being a powerful modulator of BCR signaling that may play an important role in normal and malignant B cells.

L18 ANSWER 4 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2002:199074 Document No.: PREV200200199074. Gene expression profiling in two forms of acute leukemia involving the AML1 gene: Comparison to normal CD34+ progenitor cells. Hokland, Peter [Reprint author]; Thykjaer, Thomas; Orntoft, Torben; Holm, Mette Skov [Reprint author]; Pallisgaard, Niels [Reprint author]. Hematology, Aarhus University Hospital, Aarhus, Denmark. Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 566a. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB Acute leukemias can be divided into lymphoid (ALL) and myeloid (AML) according to standard diagnostic criteria, most notably immunophenotyping. However, underlying this classification is a remarkable heterogeneity, as evidenced by the increasing number of recurrent chromosome abnormalities found in these disorders, especially balanced translocations. Moreover, despite a widening knowledge of the genes involved in such genetic lesions, little is known about leukemic processes. We have employed oligonucleotide-based DNA microarrays to study the global gene expression of more than 6600 genes in 3 cases of TEL/AML+ (t(12;21)) pre-B ALL and in 3 cases of AML/ETO+ (t(8;21)) AML. When gene expression was compared in these two disorders, which both involve the AML gene on chromosome 21, we found them to be clearly distinct from each other and from mobilized CD34+ cells from normal donors, with AML/ETO+ cases resembling normal CD34+ more than the TEL/AML ones. In the TEL/AML+ patients, 165 genes were either more than 3-fold increased or decreased compared to normal CD34+ cells. For ETO/AML+ patients the number was 93. A striking homogeneity within the patient groups and the normal CD34+ cells was common to all gene expression alterations, probably reflecting the fact that focused subsets within AML and ALL patients were chosen a priori. Categorizing genes

according to cellular function revealed that a number of genes already known to exert important functions in either lymphoid or myeloid cells were differentially expressed. Thus, while such genes as CD10, CD19, CD79alpha (MB-1) and IL-7R were more than 10-fold overexpressed in TEL/AML+ cases, a range of enzymes related to myeloid cell function such as myeloperoxidase, elastase and proteinase-3 were all more than 20-fold overexpressed in AML/ETO. More importantly, however, was the unexpected finding that some heat-shock proteins were clearly downregulated in both TEL/AML and AML/ETO, most notably hsp40 (8 and 30 fold, respectively) and hsp70 (59 and 47 fold, respectively). Interestingly, hsp27, which has previously been found to be upregulated in some forms of pre-B ALL, was unaltered in both patient groups. In addition, a series of transcription factors were differentially regulated between the subgroups, while a group of cell cycle related genes were upregulated in AML/ETO+ cells compared to both TEL/AML+ and normal CD34+ cells. Finally, 11 number genes with unknown function (ESTs) were been identified. The magnitude of gene expression alterations identified by the chip methodology was validated in separate patients employing TaqMan real-time quantitative PCR with the exception of CD10 (CALLA), which was found to be 100-fold more expressed in the RQ-PCR assay. We conclude that focused gene expression profiling is a valuable tool to distinguish subsets of acute leukemias already characterized by distinct chromosomal aberrations. Moreover, even subsets with balanced translocations studied here, which share one **fusion** partner, display remarkably dissimilar gene profiles. These data therefore form the basis for further investigations into the leukemogenesis and for refining the diagnostic processes in these diseases.

L18 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
2000:756855 Document No. 133:318803 Synthetic signal transducing proteins using motifs associated with receptor binding and activation. Lawson, Alastair David Griffiths; Finney, Helene Margaret (Celltech Therapeutics Limited, UK). PCT Int. Appl. WO 2000063372 A1 20001026, 74 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-GB1456 20000417. PRIORITY: GB 1999-8807 19990416.

AB The invention relates to synthetic signalling mols., which are based on sequences derived from primary signalling motifs such as Ig tyrosine receptor-based activation motifs (ITAMs). The use of such signalling mols. within chimeric receptor proteins allows one to tailor the level of intracellular signalling mediated by the chimeric receptor. Proteins containing, and nucleic acids encoding, such synthetic signalling mols. suitable for use in medicine, are described.

L18 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
1999:795994 Document No. 132:31744 Gene probes used for genetic profiling in healthcare screening and planning. Roberts, Gareth Wyn (Genostic Pharma Ltd., UK). PCT Int. Appl. WO 9964627 A2 19991216, 745 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1780 19990604. PRIORITY: GB 1998-12099 19980606; GB 1998-13291 19980620; GB 1998-13611 19980624; GB 1998-13835 19980627; GB 1998-14110 19980701; GB 1998-14580 19980707; GB 1998-15438 19980716; GB 1998-15576 19980718; GB 1998-15574 19980718; GB 1998-16085 19980724; GB

1998-16086 19980724; GB 1998-16921 19980805; GB 1998-17097 19980807; GB 1998-17200 19980808; GB 1998-17632 19980814; GB 1998-17943 19980819.

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the number of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide critical clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic" profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L18 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

1999:795993 Document No. 132:31743 Gene probes used for genetic profiling in healthcare screening and planning. Roberts, Gareth Wyn (Genostic Pharma Limited, UK). PCT Int. Appl. WO 9964626 A2 19991216, 149 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1779 19990604. PRIORITY: GB 1998-12098 19980606; GB 1998-28289 19981223.

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the number of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide critical clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

=> s (chang t?/au)

L19 15129 (CHANG T?/AU)

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=> s l19 and fusion
L20         208 L19 AND FUSION

=> s l20 and T cell epitope
   4 FILES SEARCHED...
L21           0 L20 AND T CELL EPITOPE

=> s l20 and Fc
L22          27 L20 AND FC

=> dup remove l22
PROCESSING COMPLETED FOR L22
L23          13 DUP REMOVE L22 (14 DUPLICATES REMOVED)

=> d l23 1-13 cbib abs

L23  ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2004 ACS on STN
2003:97801   Document No. 138:152277  Treatment of tumors and viral infections
     with a hybrid of interferon and an immunoglobulin Fc fragment.
     Yu, Liming; Chang, Tse Wen (USA).  U.S. Pat. Appl. Publ. US
     2003026779 A1 20030206, 9 pp., Cont. of U.S. Ser. No. 418,734, abandoned.
     (English).  CODEN: USXXCO.  APPLICATION: US 2001-5438 20011203.  PRIORITY:
     US 1999-418734 19991015.
AB   The authors disclose interferon-Ig Fc fusion proteins
     (referred to as "IFN-Fc hybrids").  In one example, a hybrid of
     interferon-α exhibited virus cytopathicity.  In a second example, a
     hybrid of interferon-α exhibited antitumor activity towards a
     Burkitt lymphoma xenograft in mouse.  The preferred Fc fragment
     is a human Ig Fc fragment, preferably the γ4 chain.

L23  ANSWER 2 OF 13      MEDLINE on STN                    DUPLICATE 1
2003031355.    PubMed ID: 12538671.  Comparative effects of human Ig alpha and
     Ig beta in inducing autoreactive antibodies against B cells in mice.  Sheu
     Jim J C; Cheng Tammy; Chen Huan Y; Lim Carmay; Chang Tse-Wen.
     (Department of Life Science, National Tsing Hua University, Hsinchu,
     Taiwan. ) Journal of immunology (Baltimore, Md. : 1950), (2003 Feb 1) 170
     (3) 1158-66.  Journal code: 2985117R.  ISSN: 0022-1767.  Pub. country:
     United States.  Language: English.
AB   Human and mouse Ig alpha molecules share only 58% amino acid sequence
     identity in their extracellular regions.  However, mice immunized with a
     recombinant Fc fusion protein containing the
     extracellular portion of human Ig alpha produced significant amounts of
     IgG capable of binding to Ig alpha on mouse B cells.  The induced
     auto/cross-reactive Abs could down-regulate B cell levels and the
     consequent humoral immune responses against an irrelevant Ag in treated
     mice.  Analogous immunization with an Fc fusion
     protein containing the extracellular portion of human Ig beta gave a much
     weaker response to mouse Ig beta, although human and mouse Ig beta, like
     their Ig alpha counterparts, share 56% sequence identity in their
     extracellular regions.  Protein sequence analyses indicated that a
     potential immunogenic segment, located at the C-terminal loop of the
     extracellular domain, has an amino acid sequence that is identical between
     human and mouse Ig alpha.  A mAb A01, which could bind to both human and
     mouse Ig alpha, was found to be specific to a peptide encompassing this
     immunogenic segment.  These findings suggest that specific
     auto/cross-reactivity against self Ig alpha can be induced by a molecular
     mimicry presented by a foreign Ig alpha.

L23  ANSWER 3 OF 13      MEDLINE on STN                    DUPLICATE 2
2002459345.    PubMed ID: 12218370.  Monoclonal antibodies against the
     C(epsilon)mX domain of human membrane-bound IgE and their potential use
     for targeting IgE-expressing B cells. Chen Huan Yuan; Liu Fu-Tong; Hou
     Charlie M H; Huang Janice S W; Sharma Bhavya Bhavna; Chang Tse Wen
     . (Department of Life Science, National Tsing Hua University, Hsinchu,
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Taiwan, ROC.) International archives of allergy and immunology, (2002 Aug) 128 (4) 315-24. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: IgE mediates immediate-type hypersensitivity reactions responsible for various allergic symptoms. It is secreted by IgE-producing plasma cells, which differentiate from B cells expressing membrane-bound IgE (mIgE) on their surface. The epsilon-chain of human mIgE contains a membrane-anchoring peptide and an extra 52-amino-acid (a.a.)-long domain (referred to as C(epsilon)mX) between the membrane anchor and the CH4 domain. OBJECTIVE: The study was designed to evaluate the effects of C(epsilon)mX-specific monoclonal antibodies (mAbs) to target IgE-expressing B cells and decrease IgE production. METHODS: A C(epsilon)mX-containing IgG1.**Fc fusion** protein was produced in CHO cells and used to immunize mice; five hybridoma clones secreting C(epsilon)mX-specific mAbs were obtained. RESULTS: Characterization of the mAbs using ELISA, immunoprecipitation, and immunoblotting methods showed that they could bind to both native and denatured forms of C(epsilon)mX. The mAbs exhibited mutual inhibition of binding to mIgE. Epitope mapping using synthetic peptides revealed that all five mAbs recognize the same epitope, RADWPGPP, located near the C-terminus of C(epsilon)mX. Binding of one of the mAbs to mIgE on SKO-007 cells induced the cross-linking of mIgE molecules on the cell surface, resulting in their patching and capping. In vitro functional analysis revealed that mAbs are able to cause complement-mediated cytotoxicity on transfectants expressing the **Fc** portion of mIgE. CONCLUSION: We have prepared several human mIgE-specific mAbs. The potential of the mAbs on targeting mIgE+ B cells was demonstrated by CDC analysis.

L23 ANSWER 4 OF 13 MEDLINE on STN DUPLICATE 3

2002207068. PubMed ID: 11941453. Inducing specific reactivity against B cells in mice by immunizing with an **Fc fusion** protein containing self-Igbeta. Sheu Jim J C; Huang Janice; **Chang Tse W.** (Department of Life Science, National Tsing Hua University, Hsinchu 300, Taiwan.) Cancer immunology, immunotherapy : CII, (2002 May) 51 (3) 145-52. Journal code: 8605732. ISSN: 0340-7004. Pub. country: Germany: Germany, Federal Republic of. Language: English.

AB A recombinant chimeric **fusion** protein, muIgbeta-hugamma4.**Fc**, composed of the extracellular domain of mouse Igbeta (CD79b) and the CH2-CH3 domains of human IgGgamma4.**Fc** (hugamma4.**Fc**), linked via an immunologically inert flexible peptide, was prepared. The **fusion** protein was evaluated for its ability to induce specific auto-reactive immune response against Igbeta and to modulate B cell activity in Balb/c mice. Upon immunization with muIgbeta-hugamma4.**Fc**, mice developed immunoglobulin (IgG) against self-Igbeta, which could bind to the cells of a mouse B cell line expressing Igbeta on the cell surface. The proportion of B cells in mononuclear cells in the peripheral blood (PBMC) of treated mice decreased as compared to that of mice immunized with hugamma4.**Fc** without the Igbeta component. Furthermore, mice immunized against muIgbeta-hugamma4.**Fc** displayed a reduced antibody response against an irrelevant antigen. The implications of employing the present approach in developing a therapeutic strategy for regulating B cell activity has been discussed.

L23 ANSWER 5 OF 13 MEDLINE on STN DUPLICATE 4

2002140847. PubMed ID: 11841845. Down regulation of B cells by immunization with a **fusion** protein of a self CD20 peptide and a foreign IgG.**Fc** fragment. Huang Janice; Sheu Jim Jinn Chyuan; Wu Stanley Chi Shen; **Chang Tse Wen.** (College of Life Science, National Tsing Hua University, Hsinchu, Taiwan, ROC.) Immunology letters, (2002 Apr 1) 81 (1) 49-58. Journal code: 7910006. ISSN: 0165-2478. Pub. country: Netherlands. Language: English.

AB In vivo studies of mice were performed to investigate whether auto-reactive antibodies specific for self CD20 antigen on B cells could

be induced by immunizing with a CD20 peptide linked to a foreign, human IgG.**Fc** fragment through a T cell immunologically inert linker peptide and how such an auto-reactivity, if generated, would affect the levels of B cells. The dimeric **Fc fusion** protein containing the extracellular 44-amino acid portion of CD20, and the CH2-CH3 domains of human gamma 1 immunoglobulin were prepared. After several subcutaneous immunizations with this CD20-**Fc** protein, mice produced anti-CD20 antibodies that can bind to native CD20 on normal B cells and B-lymphoma cells. In mice immunized with the CD20-**Fc** protein, the fraction of B cells in total peripheral blood lymphocytes decreased to about 40%, significantly lower than that of mice immunized with human IgG. In addition, antibody response towards an irrelevant bystander antigen, chicken ovalbumin, was weakened compared with that of mice immunized with human IgG. These results show that auto-reactive antibodies specific for CD20 can be induced by immunizing with an autologous CD20 peptide fused with a foreign IgG.**Fc** and that the auto-antibodies can partially reduce the levels of B cells and their response to other antigens.

L23 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
2001:833122 Document No. 135:370622 Induction of a humoral immune response against self-antigens. **Chang, Tse W.**; Sheu, Jim J. C.; Huang, Janice S. W.; Wu, Stanley C. S.; Chen, Leslie Y. Y. (National Tsing Hua University, Taiwan). PCT Int. Appl. WO 2001085205 A1 20011115, 75 pp. DESIGNATED STATES: W: AU, CN, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US12997 20000511.

AB The authors disclose the application of chimeric immunogens to be used as a vaccine to induce active auto-immunity specifically through a T cell-dependent antibody response. The induced autoantibodies can recognize self-antigen in vivo and trigger immune responses to reduce or eliminate a target autologous antigen. In one example, mice were immunized with a **fusion** protein comprising the extracellular domain of mouse Ig-β and a human **Fc** fragment. Following immunization, B-cell levels were shown to be significantly lower compared to controls.

L23 ANSWER 7 OF 13 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2001:314857 Document No.: PREV200100314857. Generation and characterization of monoclonal antibodies against a segment (epsilonm67) uniquely present in membrane-bound IgE. Chen, Huan Yuan [Reprint author]; Hou, Charlie M.-H.; Huang, Janice S. W.; Liu, Fu-Tong [Reprint author]; **Chang, Tse-Wen** . La Jolla Institute for Allergy and Immunology, 10355 Science Center Drive, San Diego, CA, 92121, USA. FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1018. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001. Orlando, Florida, USA. March 31-April 04, 2001.
CODEN: FAJOEC. ISSN: 0892-6638. Language: English.

AB IgE mediates immediate-type hypersensitivity and causes various allergic symptoms. IgE is secreted by IgE-producing plasma cells which are differentiated from B cells expressing IgE on the cell surface. The membrane-bound IgE (mIgE) on human B cells contains a membrane anchoring peptide and an extra 52 a.a.-long domain (referred to as CepsilonrnX) between the 15 a.a.-long exterior segment of the membrane anchor and the CH4 domain. The contiguous 67 a.a. region (referred to as epsilonm67 peptide) is mIgE-specific and can serve as a unique antigenic target for immunological intervention. In recent years, humanized anti-IgE antibodies, which can neutralize IgE and decrease IgE levels in the blood, have been shown in multiple Phase II and III trials to be safe and efficacious in treating patients with allergic rhinitis and asthma. We are developing a strategy to decrease serum IgE, by using specific monoclonal antibodies against epsilonm67 and hence IgE-expressing B cells. We have prepared an IgG1.Fcepsilonm67 **fusion** protein in Chinese hamster ovary(CHO) cells, in which epsilonm67 exists as a dimer and thus

should resemble the native conformation. Balb/c mice were immunized with the **fusion** protein, their spleen cells were fused with the myeloma cells(NSO), and hybridomas producing mAbs against epsilonm67 were selected by ELISA. Seven hybridomas obtained from the screening were injected into Balb/c mice to produce mAb-containing ascites and the mAbs were purified by protein G column. These mAbs can bind mIgE.**Fc** -expressing transfectomas(N6m-9) as well as mIgE-expressing human myeloma cells (SKO-007). The binding characteristics were assessed by ELISA, flow cytometry and western blotting. These mAbs were shown to mediate complement-dependent cytolysis of mIgE.**Fc**-expressing transfectomas in the presence of rabbit serum complement and second antibodies (rabbit anti-mouse IgG).

L23 ANSWER 8 OF 13 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
2000:191695 The Genuine Article (R) Number: 287WR. Down-regulation of B cells in mice by active immunization with a **fusion** protein of mouse CD20 peptide and human IgG.**Fc**. Huang J S W (Reprint); Wu S C S; Chen H Y; **Chang T W.** NATL TSING HUA UNIV, DEPT LIFE SCI, HSINCHU, TAIWAN. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (JAN 2000) Vol. 105, No. 1, Part 2, Supp. [S], pp. 316-316. Publisher: MOSBY-YEAR BOOK INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318. ISSN: 0091-6749. Pub. country: TAIWAN. Language: English.

L23 ANSWER 9 OF 13 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2000:140028 Document No.: PREV200000140028. Down-regulation of B cells in mice by active immunization with a **fusion** protein of mouse CD20 peptide and human IgG.**Fc**. Huang, J. S. W. [Reprint author]; Wu, S. C. S. [Reprint author]; Chen, H.-Y. [Reprint author]; **Chang, T. W.** [Reprint author]. Department of Life Science, National Tsing Hua University, Hsinchu, Taiwan. Journal of Allergy and Clinical Immunology, (Jan., 2000) Vol. 105, No. 1 part 2, pp. S106. print.
Meeting Info.: 56th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. San Diego, California, USA. March 03-08, 2000. American Academy of Allergy, Asthma and Immunology.
CODEN: JACIBY. ISSN: 0091-6749. Language: English.

L23 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
1999:354301 Document No. 131:4242 Interferon-β **fusion** protein with immunoglobulin **Fc** fragment. **Chang, Tse Wen**; Yu, Liming (Tanox, Inc., USA). U.S. US 5908626 A 19990601, 7 pp., Cont.-in-part of U.S. 5,723,125. (English). CODEN: USXXAM. APPLICATION: US 1997-994719 19971219. PRIORITY: US 1995-579211 19951228; US 1996-719331 19960925.
AB The authors disclose a hybrid recombinant protein consisting of human interferon-β and an Ig **Fc** fragment (preferably γ4 chain) joined by a peptide linker. The hybrid mol. has increased circulatory half-life.

L23 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
1998:157344 Document No. 128:216372 Hybrid with interferon-alpha and an immunoglobulin **Fc** linked through a non-immunogenic peptide. **Chang, Tse Wen**; Yu, Liming (Tanox Biosystems, Inc., USA). U.S. US 5723125 A 19980303, 8 pp., Cont.-in-part of U.S. Ser. No. 579,211, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1996-719331 19960925. PRIORITY: US 1995-579211 19951228.
AB Disclosed is a hybrid recombinant protein consisting of human interferon, preferably interferon-α (IFNα), and human Ig **Fc** fragment, preferably γ4 chain, joined by a peptide linker comprising the sequence Gly Gly Ser Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser (SEQ ID NO:1). Plasmid pCDNA3/IFNα- **Fc** encoding the disclosed chimeric interferon-α/Ig γ4 was prepared The chimeric interferon α is useful for treating inflammatory, viral and malignant diseases.

L23 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

1997:537567 Document No. 127:148349 Hybrid with interferon-α and an immunoglobulin **Fc** linked through a non-immunogenic peptide. **Chang, Tse Wen**; Yu, Liming (Tanox Biosystems, Inc., USA). PCT Int. Appl. WO 9724137 A1 19970710, 21 pp. DESIGNATED STATES: W: AU, BB, BG, BR, CA, CN, CZ, FI, HU, JP, KP, KR, LK, LU, MG, MN, MW, NO, PL, RO, RU, SD, SG, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US20861 19961213. PRIORITY: US 1995-579211 19951228; US 1996-719331 19960925.

AB Disclosed is a hybrid recombinant protein consisting of human interferon, preferably interferon-α (IFNα), and human Ig **Fc** fragment, preferably γ4 chain, joined by a peptide linker comprising the sequence Gly-Gly-Ser-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser. The hybrid mol. is useful for treating hepatitis, hairy cell leukemia, multiple myeloma, other cancers, or viral diseases.

L23 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

1993:5605 Document No. 118:5605 Monoclonal antibodies which bind to secreted and membrane-bound IgE, but not to IgE on basophils. **Chang, Tse Wen**; Davis, Frances M.; Gossett, Lani A.; Sun, Lee K.; Sun, Bill N. C.; Sun, Cecily R. Y.; Liou, Ruey S. (Tanox Biosystems, Inc., USA). PCT Int. Appl. WO 9217207 A1 19921015, 22 pp. DESIGNATED STATES: W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US; RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1991-US1991 19910326.

AB Murine monoclonal antibody (MAb) TES-C21 and chimeric mouse/human MAb TESC-2, which has variable regions derived from TES-C21 and human (γ1,κ) constant regions, are disclosed which bind specifically to IgE and IgE-secreting B-cells. Neither MAb binds to IgE bound to IgE **Fc**.epsilon.RII receptors and both inhibit the binding of IgE to **Fc**.epsilon.RII receptors on B-cells. Neither MAb induces histamine release from human basophils. TESC-2 inhibits the binding of IgE to basophils. These properties make these MAbs well-suited for use in human allergy therapy.

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---Logging off of STN---

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Executing the logoff script...

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FULL ESTIMATED COST	187.47	187.68

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